

Serial No. 10/782,436  
Amendment Dated 11/18/2004  
Reply to Office Action of 08/25/2004

**Amendments to the Specification:**

Please replace the paragraph beginning on page 1, line 7 of the specification with the following amended paragraph:

**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a divisional application and claims the benefit of U.S. Application Serial No. 09/589,510 filed June 7, 2000, now U.S. Patent 6,706,949, which claims benefit of ~~and~~ U.S. Application Serial No. 60/144,112 filed July 16, 1999, both of which are herein incorporated by reference.

Please replace the paragraph beginning on page 19, line 24 of the specification with the following amended paragraph:

Software for performing BLAST analyses is publicly available, *e.g.*, through the National Center for Biotechnology Information (see NCBI website at [www.ncbi.nlm.nih.gov/](http://www.ncbi.nlm.nih.gov/)). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length *W* in the query sequence, which either match or satisfy some positive-valued threshold score *T* when aligned with a word of the same length in a database sequence. *T* is referred to as the neighborhood word score threshold. These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters *M* (reward score for a pair of matching residues; always > 0) and *N* (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the

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cumulative alignment score falls off by the quantity  $X$  from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters  $W$ ,  $T$ , and  $X$  determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength ( $W$ ) of 11, an expectation ( $E$ ) of 10, a cutoff of 100,  $M=5$ ,  $N=-4$ , and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength ( $W$ ) of 3, an expectation ( $E$ ) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915).

Please replace the paragraph beginning on page 69, line 16 of the specification with the following amended paragraph:

Gene identities were determined by conducting BLAST (Basic Local Alignment Search Tool; Altschul, S. F., et al., (1990) *J. Mol. Biol.* 215:403-410; see also NCBI website ~~www.ncbi.nlm.nih.gov/BLAST/~~) searches under default parameters for similarity to sequences contained in the BLAST "nr" database (comprising all non-redundant GenBank CDS translations, sequences derived from the 3-dimensional structure Brookhaven Protein Data Bank, the last major release of the SWISS-PROT protein sequence database, EMBL, and DDBJ databases). The cDNA sequences were analyzed for similarity to all publicly available DNA sequences contained in the "nr" database using the BLASTN algorithm. The DNA sequences were translated in all reading frames and compared for similarity to all publicly available protein sequences contained in the "nr" database using the BLASTX algorithm (Gish, W. and States, D. J. *Nature Genetics* 3:266-272 (1993)) provided by the NCBI. In some cases, the sequencing data from two or more clones

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containing overlapping segments of DNA were used to construct contiguous DNA sequences.